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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/921,060	08/29/1997	DARRELL R. ANDERSON	012712-432	9119

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PILLSBURY WINTHROP LLP
1600 TYSONS BOULEVARD
McLEAN, VA 22102

EXAMINER	
SCHWADRON, RONALD B	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 12/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/921,060	ANDERSON ET AL.	
	Examiner	Art Unit	
	Ron Schwadron, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24,31-34 and 41-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24,31-34 and 41-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. Applicant's election with traverse of the species method of claim 44 in the reply filed on 4/26/2004 is acknowledged. The traversal is on the ground(s) that are stated in said response. This is not found persuasive because the aforementioned methods use different antibodies with different sequences which are chemically distinct. However, the elected species has been found free of the prior art, so the search has been extended to the nonelected species.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 24,31-34,41-44 are under consideration.

3. References not considered on the enclosed PTO-1449s were already of record on a previously filed PTO-1449.

4. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP 602.01 and 602.02.

The oath or declaration is defective because It does not identify the citizenship of each inventor. The citizenship of Inventors Hanna and Newman has been omitted.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. The rejection of claims 24,31-34,41,42 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for the reasons elaborated in paragraph 5 of the Office Action mailed 9/8/2003 is withdrawn in view of the amended claims.

7. Claims 31 and 32 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants arguments have been considered and deemed not persuasive.

There is no support in the specification as originally filed for the claimed methods. The specification discloses use of the C2B8 chimeric antibody which contains the heavy and light chains recited in claims 31 and 32. However there is no disclosure in the specification of chimeric antibodies which contain the heavy chain of claim 31 in combination with any light chain per se wherein the antibody has the functional properties recited in the claim. Similarly, there is no disclosure in the specification of chimeric antibodies which contain the light chain of claim 32 in combination with any heavy chain per se wherein the antibody has the functional properties recited in the claim. There is no written description of the scope of the claimed inventions in the specification as originally filed (eg. the claimed inventions constitute new matter).

Regarding applicants comments, the specification discloses use of the C2B8 chimeric antibody which contains the heavy and light chains recited in claims 31 and 32. However there is no disclosure in the specification of chimeric antibodies which contain the heavy chain of claim 31 in combination with any light chain per se wherein the antibody has the functional properties recited in the claim. Similarly, there is no disclosure in the specification of chimeric antibodies which contain the light chain of claim 32 in combination with any heavy chain per se wherein the antibody has the functional properties recited in the claim. Regarding the various cited passages of the specification to which applicant refers, said passages fail to describe the claimed antibodies which encompass an antibody which expresses the heavy chain recited in claim 31 in combination with a nonSEQ. ID. No.7 light chain. Similarly, said passages fail to describe the claimed antibodies which encompass an antibody which expresses the light chain recited in claim 32 in combination with a nonSEQ. ID. No.11 heavy chain.

8. Claims 24,31-34,41-44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject

matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

There is no support in the specification as originally filed for the recitation of "greater than 90%" in the context recited in claim 24. Regarding applicants comments about Figure 9a and pages 49 and 51 of the specification, said portions of the specification refer to results obtained using the C2B8 chimeric antibody. Said results do not provide support for the scope of the written description of the claimed invention which encompasses any antiCD20 antibody with the particular functional results recited in the claim. The specification discloses that C2B8 has the aforementioned property but does not disclose a generic antiCD20 antibody with said property. Further, none of the passages cited disclose the limitation "greater than 90%" in the context recited in the claim. It is also noted that the aformentioned passages of the specification disclose particular experiments performed in monkeys not humans wherein the claimed invention encompasses a method of treating humans. Page 15 of the specification also does not disclose the particular limitation under consideration.

There is no written description of the scope of the claimed inventions in the specification as originally filed (eg. the claimed inventions constitute new matter).

There is no support in the specification as originally filed for the antibody of claim 44. The antibody of claim 44 encompasses antibodies with human framework regions or murine framework regions other than those found in SEQ. ID. NO;7 or 11, but there is no disclosure in the specification as originally filed of such antibodies. Regarding applicants comments about figures 4 and 5, the aforementioned antibodies (with human framework regions or murine framework regions other than those found in SEQ. ID. NO;7 or 11) are not disclosed in said Figures.

There is no written description of the scope of the claimed inventions in the specification as originally filed (eg. the claimed inventions constitute new matter).

9. The rejection of claims 24,31-34,41,42 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement for the reasons elaborated in

paragraph 7 of the Office Action mailed 9/8/2003 is withdrawn in view of the amended claims.

10. The rejection of claims 24,31-34,41,42 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the reasons elaborated in the Office Action mailed 9/8/2003 is withdrawn in view of the amended claims.

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 24,33,34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Press et al. (Blood) in view of Hellstrom et al. (WO 92/07466) and Robinson et al. (US Patent 5,500,362) or Robinson et al. (WO 88/04936).

Press et al. teach the use of a murine anti-CD20 antibody (see abstract) for the treatment of B cell lymphoma. Press et al. teach that therapeutic anti-CD20 antibody was administered to patients that had received at least one chemotherapeutic agent including cyclophosphamide(see page 586, column 1). Press et al. teach the use of murine anti-CD20 antibody wherein said antibody depletes greater than 90%peripheral B cells within 24 hours at a dosage less than that recited in the claim(see Figure 2).

The first dosage used in Press et al., figure 2 is approximately 10mg/hypothetical 75kg human whilst the functional dosage recited in claim 24 is approximately 30 mg/hypothetical 75kg human). Press et al. does not teach that the method uses a chimeric antibody with the functional property recited in the claims. While the murine antibody taught by Press et al. has the functional properties recited in claim 24, Robinson et al. teach that it would be expected that a chimeric anti-CD20 antibody would have greater lytic activity in vivo compared to the murine antibody from which it is derived, because the chimeric antibody would possess increased ADCC and CDC (see column 20 or page 43). Hellstrom et al. teach that chimeric antibodies have increased immune function because they contain human Fc (see page 13). Hellstrom et al. teach use of antitumor antibodies in combination with chemotherapeutic agents such as doxorubicin (see abstract). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Press et al. teaches the use of antiCD20 antibody to treat B cell lymphoma, while Hellstrom et al. teach chimeric monoclonal antibody treatment in combination with chemotherapeutic agents can be used to treat cancer and Robinson et al. teach the use of chimeric antiCD20 antibody to treat B cell lymphoma and the advantages of using such antibodies. One of ordinary skill in the art would have been motivated to do the aforementioned because Hellstrom et al. teach the use of chimeric antibodies in combination with chemotherapy (see page 7) and Robinson et al. teach the use of chimeric anti-CD20 antibody for the treatment of B cell lymphoma (see column 20).

13. Claims 41,42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Press et al. (Blood) in view of Hellstrom et al. (WO 92/07466) and Robinson et al. (US Patent 5,500,362) or Robinson et al. (WO 88/04936)as applied to claims 24,33,34 above, and further in view of Eary et al.

The previous rejection renders obvious the claimed invention except for the methods of claims 41,42. Eary et al. disclose use of radiolabelled antiCD20 antibody for the diagnostic evaluation of tumor cell mass before treatment with an antiCD20 antibody

(see pages 1259-1263). The diagnostic treatment provides an estimate of tumor mass before treatment. Post therapy imaging with radiolabelled antibody provides an estimate of tumor mass after treatment (see page 1265, second column, first two paragraphs). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because the previous rejection renders obvious the claimed invention except for the methods of claims 41,42, whilst Eary et al. disclose use of radiolabelled antiCD20 antibody for the diagnostic evaluation of tumor cell mass before and after treatment with an antiCD20 antibody. One of ordinary skill in the art would have been motivated to do the aforementioned to assess the efficacy of the antiCD20 therapeutic treatment.

14. No claim is allowed.

15. Applicant's amendment and information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ron Schwadron, Ph.D. whose telephone number is 571 272-0851. The examiner can normally be reached on Monday-Thursday 7:30-6:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RONALD B. SCHWADRON
PRIMARY EXAMINER
GROUP ~~1800~~ 1600

Ron Schwadron, Ph.D.
Primary Examiner
Art Unit 1644